

levels of CTGF and TGF- β will induce recruitment of myofibroblasts and provoke adventitial reorganization to limit outward remodeling of the vein graft in response to increased intramural wall stress.

The authors created a model using a distal arterial venous fistula in the neck of rabbits that results in circumferential wall shear stress. Neck and fistula veins were harvested at 1, 3, and 7 days after implantation. Flow rates were recorded at the time of graft implantation and harvest using an ultrasonic flow meter. Real-time polymerase chain reaction and enzyme-linked immunosorbent assays were used to assess production of CTGF and TGF- β .

With this model, the authors demonstrated increased production of TGF- β and CTGF in response to elevated wall stress. TGF- β and CTGF increased expression correlated with enhanced differentiation from fibroblasts to myofibroblasts, as reflected in increases in the α -actin-positive cells in the adventitia. Levels of α -actin, TGF- β , and CTGF were all inversely correlated with outward remodeling of the graft wall.

Comment: Wolinsky and Glagov originally demonstrated arterial adaption to maintain lumen diameter in atherosclerotic arteries. In vein grafts, this adaptive response might be limited by TGF- β and CTGF increases in myofibroblasts. Such an adaption may maintain vein wall integrity in the face of increased intraluminal pressure but may ultimately prove disadvantageous because it may limit the ability of the vein graft to maintain luminal diameter in response to the development of intimal hyperplasia.

Temporary worsening of renal function after aortic surgery is associated with higher long-term mortality

Welten GM, Schouten O, Chonchol M, et al. *Am J Kidney Dis* 2007;50:219-28.

Conclusion: Temporary worsening of renal function after open surgery for abdominal aortic aneurysm (AAA) is associated with an increased long-term mortality rate.

Summary: The authors sought to determine the effects of temporary renal dysfunction on the long-term mortality rate in patients undergoing AAA surgery. From January 1995 to June 2006, 1324 patients underwent elective open AAA repair in a single center in Rotterdam. Creatinine clearance was measured preoperatively and on postoperative days 1, 2, and 3. The patients were then divided into three groups. Group 1 had improved or unchanged renal function. Group 2 had temporary worsening of renal function with a $>10\%$ decrease on day 1 or 2, and then recovery $\leq 10\%$ of baseline by day 3. Group 3 patients had persistent worsening of renal function as defined by a $>10\%$ decrease in creatinine clearance compared with the baseline value.

The 30-day mortality rates in groups 1, 2, and 3 were 1.2%, 5%, and 12.6%, respectively. Adjusting for postoperative complications and baseline characteristics, the 30-day mortality rate was greatest in the patients with persistent worsening of renal function (hazard ratio (HR), 7.3; 95% confidence interval [CI], 2.7-19.8). Those who had temporary worsening of renal function also had an increased mortality risk (HR, 3.7; 95% CI, 1.4-9.9). Follow-up was for 6.0 ± 3.4 years. During follow-up, 348 patients (36.5%) died. The HR for late death was 1.7 (95% CI, 1.3-2.3) in the patients who had persistent worsening of renal function. For those who had temporary worsening of renal function, the HR for death was 1.5 (95% CI, 1.2-1.4). There was a significant association between perioperative blood loss and worsening of renal function ($P < .001$) and between length of suprarenal aortic clamping and worsening of renal function ($P < .001$). There was also a greater incidence of hypertension in the patients with temporary and persisting renal dysfunction ($P < .001$).

Comment: Another recent study suggested minimal changes in renal function after cardiothoracic surgery had little impact on long-term prognosis (*J Am Soc Nephrol* 2004;15:1597-605). The current study reaches an opposite conclusion. Although this study was retrospective, the mean follow-up was long (6 years) and the number of patients was large ($n = 1324$). It is reasonable, therefore, to conclude that any significant worsening of perioperative renal function in an AAA patient carries an adverse prognosis both in the near- and long-term. Although it seems nice when transient renal dysfunction after AAA surgery returns to baseline levels, it doesn't appear to do the patient any good.

Effects of random allocation to vitamin E supplementation on the occurrence of venous thromboembolism: Report from the Women's Health Study

Glynn RJ, Ridker PM, Goldhaber SZ, et al. *Circulation* 2007;116:1497-503.

Conclusion: Vitamin E supplementation lowers the risk of venous thromboembolism (VTE).

Summary: Vitamin E supplementation may serve as a natural antagonist of vitamin K in healthy adults. Whether vitamin E can sufficiently antagonize vitamin K activity to decrease the risk of VTE is unknown. The Women's Health Study tested the effects of vitamin E supplementation for

10 years on the risk of cardiovascular disease or cancer in a large group of women without these diseases at study entry. The study randomized 39,876 women aged ≥ 45 years to receive 600 IU of vitamin E, or placebo, on alternate days. Before randomization, blood samples were obtained from 26,779 participants to determine G20210A prothrombin gene mutation, factor V Leiden, and 5,10 methylenetetrahydrofolate reductase (MTHFR) gene polymorphisms. The authors evaluated development of unprovoked VTE (no known diagnosis of cancer and no recent surgery or trauma).

During a median follow-up of 10.2 years, VTE developed in 482 women, 213 in the vitamin E group and 269 in the placebo group, a 21% hazard reduction in the vitamin E group (relative hazard, 0.79; 95% confidence interval [CI], 0.66-0.94; $P = .010$). For unprovoked VTE, the hazard reduction was 27% (relative hazard, 0.73; 95% CI, 0.57-0.94; $P = .016$). A subgroup analysis of the 3% of women in the study who reported VTE before randomization found they had a 44% hazard reduction (relative hazard, 0.56; 95% CI, 0.31-1.00; $P = .048$) with vitamin E supplementation. Women without prior VTE had an 18% hazard reduction (relative hazard, 0.82; 95% CI, 0.68-0.99; $P = .040$). In women with either the prothrombin gene mutation or factor V Leiden, the hazard reduction was 49% with vitamin E treatment (relative hazard, 0.51; 95% CI, 0.30-0.87; $P = .014$).

Comment: The Women's Health Study itself, and many recent meta-analysis, have not supported a recommendation for vitamin E supplementation to reduce overall cardiovascular events (*JAMA* 2005;295:56-65 and *Lancet* 2003;361:2017-2023). The finding that vitamin E supplementation may prevent VTE is, however, not at odds with these previous observations. Arterial and venous events may not share similar mechanisms in all cases. Given the size of this study and its prospective nature, it does appear vitamin E may lower the risk of VTE, especially in women with genetic risk factors.

Seasonal variation in surgical outcomes as measured by the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP)

Englesbe MJ, Pelletier SJ, Magee JC, et al. *Ann Surg* 2007;246:456-65.

Conclusion: There are seasonal variations in surgical outcomes with respect to postoperative morbidity and mortality.

Summary: The complete experience of a surgical procedure is complex and involves interactions between both systems and individuals. It is assumed that increased surgeon experience can help produce favorable outcomes. In July and August, there are relatively new trainees in most academic medical centers. At this time of the year, the trainees are less familiar with their roles and responsibilities. It is postulated there may be more adverse outcomes in surgical procedures performed early in the academic year vs later. The authors propose that the National Surgical Quality Improvement Program (NSQIP) is a database that is sufficiently large to allow a multi-center, risk-adjustment analysis of surgical morbidity and mortality on a month-to-month basis. In this study, the authors use 30-day morbidity and mortality rates derived from NSQIP-participating hospitals and compared two periods of care: an early group from July 1 to August 30 and a late group from April 15 to June 15. The postoperative morbidity rate was 18% higher in the early ($n = 9941$) vs late ($n = 10,310$) groups (odds ratio, 1.18; 95% confidence interval [CI], 1.07-1.29, $P = .0005$; c-index, 0.794). Mortality was 41% higher in the early group compared with the late group (odds ratio, 1.41; 95% CI, 1.11-1.80; $P = .005$; c-index 0.938).

Comment: The study really cannot reliably implicate inexperience of resident trainees as contributing to the so-called July effect. No hospitals without training programs were included as controls. In addition, other studies have suggested a "July effect" does not exist (*Surgery* 2001;130:346-53 and *J Gen Intern Med* 2003;18:639-45). The authors also noted an uptake in morbidity and mortality in December. At this point, resident inexperience is not likely important. Also, many attending surgeons take a vacation in July and August; therefore, slightly more urgent cases may be performed in those months than at other times of the year. It may be that less attending supervision in peak vacation months or more urgent surgery in the summer months and December are contributing more to seasonal variation in surgical morbidity and mortality than the inexperience of resident physicians.

The female advantage in cardiovascular disease: Do vascular beds contribute equally?

Kardys I, Vliegghart R, Oudkerk M, et al. *Am J Epidemiol* 2007;166:403-12.

Conclusion: There is a larger gender difference in atherosclerosis of the coronary vessels than in other vascular beds, with women having less severe disease than men. There are no gender differences in the aorta and lower extremity vessels.

Summary: It is widely acknowledged that women have less incidence of coronary heart disease than men. In this study, the authors sought to characterize gender differences in cardiovascular disease according to vascular site. Degrees of coronary, carotid, peripheral, and aortic atherosclerosis were compared in men and women aged >55 years from the population-based Rotterdam Study. The study used data collected between 1997 and